Remarks

I. Status of the Application and Claims

As originally filed, the present application had a total of 18 claims. Claims 1-11and 18-29 have been cancelled herein. Thus, the claims now pending are claims12-17.

II. The Amendments

Claims 1-11 and 18-29 have been cancelled. Apart from this, claim 12 has been amended to define the abbreviation "COX-2" and to indicate that the labeling in therapeutic packages is directed to the use of the drug combination by all patients. As discussed more fully in the Arguments section, this reflects that fact that anyone taking COX-2 specific NSAIDs is at increased risk of experiencing a thromboembolic event, not just patients with preexisting cardiovascular problems.

The amendments made herein do not add new matter to the application and their entry is therefore respectfully requested.

III. Claim Objections

On page 2 of the Office Action, the examiner objects to the use of the abbreviation "COX-2" in claims without first properly identifying it. In response, Applicant uses the full term"cyclooxygenase-2" to define the abbreviation in amended claim 12. It is therefore submitted that the Examiner's objection has been overcome.

The Rejections

On pages 2-6 of the Office Action, all pending claims are rejected under 35 USC §102 as being anticipated by Scolnick (US 2002/0016342). The Examiner argues that the Scolnick reference discloses the same combination of drugs being claimed by Applicant and that the labeling recited in therapeutic package claims does make the invention patentable because it lacks a functional relationship with the claimed product and, instead, merely represents an intended use.

Applicant respectfully traverses this rejection.

In responding, Applicant will focus exclusively on the therapeutic package claims (*i.e.*, claims 12-17) since all other claims have been cancelled. The response below first explains why there is a significant difference between the invention claimed in the application and that disclosed in Scolnick. It then discusses why labeling instructions are an integral part of the composition for pending therapeutic package claims

A. Distinguishing the Claimed Invention from Scolnick

The Examiner is correct in indicating that the Scolnick reference discloses the same drug combination as Applicant, *i.e.*, combinations that have a COX-2 NSAID inhibitor and a thromboxane A2 receptor antagonist such as ifetroban. Nevertheless, there is a significant difference between the teachings of the Scolnick reference and Applicant's teachings with respect to the way in which the drug combination is used. The reference recognizes that traditional NSAIDs inhibit COX-1 and that one consequence of this inhibition is that a protein promoting platelet aggregation is blocked (see *e.g.*, paragraph 0003 of the reference). By reducing the risk of platelet aggregation, the COX-1 inhibitors also reduce the risk of a patient experiencing an adverse cardiovascular event. This is the reason why many people take low dose NSAIDs such as aspirin. The reference also recognizes that this beneficial effect of COX-1 inhibition is lost when inhibitors specific for COX-2 are used and it suggests that people that are at risk of having a thromboembolic event can recover some of the benefits of COX-1 inhibition (without increasing the risk of developing gastrointestinal lesions) by taking a combination of a COX-2 inhibitor and a thromboxane A2 receptor antagonist (see, *e.g.*, paragraph 0007). Patients at risk of developing a thromboembolic event are defined in paragraph 0015 and are people that have either previously had such an event, have a family history of cardiovascular disease or who are otherwise at high risk because of genetic factors.

However, the reference fails to recognize that the COX-2 inhibitors, by upsetting the normal balance between COX-1 and COX-2 activity, are actually creating cardiovascular problems in people that are healthy and not at increased risk of having a stroke, or heart attack.

This is discussed, *e.g.*, on page 2 of the present application, lines 1-10. At the time that Applicant filed its application, this view was not widely held but since then, the potential heart problems arising from the chronic use of NSAIDs such as Vioxx has gotten wide attention. The view that it is the COX-2 inhibitors themselves that are creating a problem has consequences for the way that the combination of drugs is administered. In particular, it means that whenever a COX-2 inhibitor is taken, a thromboxane A2 receptor antagonist should be taken as well, whether a person is at increased risk of a thromboembolic event (as defined by Scolnick) or not. It is not just a matter of patients at increased risk of thromboembolisms losing a benefit Thus, the application suggests that the combination of drugs should be given to everyone taking COX-2 inhibitors, *i.e.*, all patients, whereas the reference only suggests administration to a subpopulation of "at risk" patients.

B. Labeling Instructions as a Basis for Patentability

Applicant has read the Examiner's comments regarding the limitations of using labeling as a means of making a known composition patentable. However this fails to take into account that labeling is an integral part of pharmaceutical packages in a way that is not the case with other products. The relevant composition is not just the drug combination but the drug combination and its approved use as set forth in the labeling. In this sense, a change in labeling does represent a structural change in the composition in a way that merely including new printed matter with other products does not. Moreover, drug products can only be labeled for uses that are approved by the FDA and the range of functions for a drug product is in fact directly affected by its labeling. Thus, using the criteria of In re Gulak, the function of a drug product does depend on the printed matter itself, *i.e.* the way that it is labeled.

A separate question is whether the Scolnick reference suggests the same labeling as Applicant has specified in the present claims. For the reasons discussed above, Applicant submits that any labeling based upon the Scolnick reference would be directed to the use of the pharmaceutical combination for patients at elevated risk of a thromboembolic event. In contrast, Applicant has suggested that *all* patients taking COX-2 inhibitors should also be taking a thromboxane A2 inhibitor and the therapeutic package claims (*i.e.* 12-17) reflect this. Thus,

Applicant submits that the claimed therapeutic packages are neither disclosed nor suggested by Scolnick.

Conclusion

In light of the amendments and discussion above, Applicant respectfully submits that all of the Examiner's rejections have been overcome. It is therefore requested that these rejections be withdrawn and that the claims presently pending in the application be allowed.

If, in the opinion of the Examiner, a phone call may help to expedite the prosecution of this application, the Examiner is invited to call Applicant's undersigned attorney at (240)864-0915.

Respectfully submitted,

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